01997.001700.



PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

ANJANA RAO, ET AL.

Application No.: 10/058,024

Filed: January 29, 2002

For: ANERGY-REGULATED

Examiner: Not Yet Assigned

AUG 0 1 2002

TECH CENTER 1600/2900

July 30, 2002

Commissioner for Patents Washington, D.C. 20231

**MOLECULES** 

## **INFORMATION DISCLOSURE STATEMENT**

Sir:

In compliance with the duty of disclosure under 37 C.F.R. § 1.56 and in accordance with the practice under 37 C.F.R. §§ 1.97 and 1.98, the Examiner's attention is directed to the documents listed on the enclosed Form PTO-1449. Copies of the listed documents are also enclosed.

It is respectfully requested that the above information be considered by the Examiner and that a copy of the enclosed Form PTO-1449 be returned indicating that such information has been considered.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our address given below.

Respectfully submitted,

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Rey RenderTECH CENTER 1600/2900 Attorney for Applicants

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		OTHER DOCUMENT(	S) (Including Author, Title, Date,	Pertinent Pages, Etc.)	1	<u> </u>		
	Heidi Okamura, et al., "Concerted Dephosphorylation of the Transcription Factor NFAT1 Induces a Conformational Switch that Regulates Transcriptional Activity", Molecular Cell, Vol. 6, pp. 539-550 (September, 2000).							
	Richard A. H	Richard A. Houghten, et al., "Generation and use of synthetic peptide combinatorial libraries for basic research and drug discovery", Nature, Vol. 354, pp. 84-86 (November 7, 1991).						
		Stefan Feske, et al., "Gene regulation mediated by calcium signals in T lymphocytes", Nature Immunology, Vol. 2, No. 4, pp. 316-324 (April 2001).						
		Jörg Heyer, et al., "Inefficient Termination of Antigen Responses in NF-ATp-Deficient Mice", Immunobiol., vol. 198, pp. 162-169 (1997).						
	Histocompat	Jan Buer, et al. "Interleukin 10 Secretion and Impaired Effector Function of Major Histocompatibility Complex Class IIrestricted T Cells Anergized In Vivo", J. Exp. Med. Volume 187, No. 2, pp. 177-183 (January 19, 1998).						
	Rakesh Datta Apoptosis", 15, 1997).	Rakesh Datta, et al., "Caspase-3-mediated Cleavage of Protein Kinase C θ in Induction of Apoptosis", The Journal of Biological Chemistry Vol. 272, No. 33, pp. 20317-20320 (August						
			rnative Polyadenylat Immunity, Vol. 10, p				ction of	
	Wei Fang, et Selection an 35-45 (July,	d Are Tolerized	ive B Lymphocytes C by Clonal Anergy an	Overexpressing d Receptor Edit	Bcl-xլ E։ ing", İmi	scape Neg munity, V	gative ol. 9, pp.	
	Dirk Eberhar corepressors (2000).	d, et al., "Trans s of the Grouch	criptional repression family", The EMBO	by Pax5 (BSAP) Journal, Vol. 19	) throug 9, No. 10	h interact , pp. 2292	ion with 2-2303	
	Johannes L. regarding in pp. 6776-678	terconnectivity (	ember's Review Al of Ras, Rap1 and Ral	I in the family? I", The EMBO Jo	New ins ournal, V	ights and ol. 17, No	questions . 23,	
			aspase-mediated Dec 22-1427, (April 1, 199		ell Rece	ptor ζ-Cha	ain",	

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<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE  LIST OF REFERENCES CITED BY APPLICANT(S) (Use several sheets if necessary)			ATTY DOCKET NO. 01997.001700	10/058,0	00 NØ . \ 1 024 O	E		
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	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES/NO/ OR ABSTRACT		
	OTHER DOCUMENT(S) (Including Author, Title, Date, Pertinent Pages, Etc.)							
		Stanford L. Reng, et al. "NFATc1 and NFATc2 Together Control Both T and B Cell Activation and Differentiation", Immunity, Vol. 14, No. pp. 13-20 (January 2001).						
	Thomas M. Y desensitizati	Thomas M. Yankee, et al., "CD95 / Fas induces cleavage of the GrpL / Gads adaptor and desensitization of antigen receptor signaling", PNAS, pp. 6789-6793 (June 5, 2001).						
	through a me	Pierangela Sabbattini, et al., "Binding of Ikaros to the λ5 promoter silences transcription through a mechanism that does not require heterochromatin formation", The EMBO Journal, Vol. 20 No. 11, pp. 2812-2822 (2001).						
	Kai Schuh, e ATp-deficien	Kai Schuh, et al., "Retarded thymic involution and massive germinal center formation in NF-ATp-deficient mice", Eur. J. Immunol. Vol. 28, pp. 2456-2466 (1998).						
	David G. Telander, et al., "Evidence for Repression of IL-2 Gene Activation in Anergic T Cells", Journal of Immunology, Vol. 162, pp. 1460-1465 (1999).  Masashi Toyoda, et al., "Jumonji Is a Nuclear Protein That Participates in the Negative Regulation of Cell Growth", Biochemical and Biophysical Research Communications, Vol. 274, pp. 332-336 (2000).							
	James I. Hea	James I. Healy, et al. "Different Nuclear Signals Are Activated by the B Cell Receptor during Positive Versus Negative Signaling", Immunity, Vol. 6, pp. 419-428 (April, 1997).						
		Martin R. Hodge, et al., "Hyperproliferation and Dysregulation of IL-4 Expression in NF-ATp-Deficient Mice", Immunity, Vol. 4, pp. 397-405 (April, 1996).						
	Shintaro Kar Proteolysis o	Shintaro Kamizono, et al., "The SOCS Box of SOCS-1 Accelerates Ubiquitin-dependent Proteolysis of TEL-JAK2", The Journal of Biological Chemistry, Vol. 276, pp. 12530-17538 (April 20, 2001).						
	Astrid Lanou	ie, et al., J. Exp. I	Med., Vol. 185, No. 3, 405-414, (Febr	uary 3, 1	997).			
	Lyudmila Lya	akh, et al., "Expre	ession of NFAT-Family Proteins in N y, p. 2475-2484 (May 1997).			Cells",		
	Xian Chang I	Li, et al., "The rol	e of T cell apoptosis in transplantat	tion tole	rance", C	urrent		
		Opinion in Immunology, Vol. 12, pp. 522-527, (2000).						
	Miguel Angel Sanjuán, et al., "Role of Diacylglycerol Kinase α in the Attenuation of Receptor Signaling", The Journal of Cell Biology, Vol. 153, No. 1, pp. 207-219 (April 2, 2001).							

**EXAMINER** 

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO 1449 (modified)  U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE  LIST OF REFERENCES CITED BY APPLICANT(S) (Use several sheets if necessary)			ATTY DOCKET NO. 01997.00	01997.001700 10/058,024			E		
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	Fernando Ma	,			ne nrese	nce or ab	sence of		
	cooperative (2000).	Fernando Macián, et al., "Gene expression elicited by NFAT in the presence or absence of cooperative recruitment of Fos and Jun", The EMBO Journal, Vol. 19, No. 17, pp. 4783-4795 (2000).							
	Stephen F. A database sea	Stephen F. Altschul, et al., "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Research, Vol. 25, No. 17, pp. 3389-3401 (1997).							
	Sheila Hobbs chemical div	Sheila Hobbs DeWitt, et al., "'Diversomers': An approach to nonpeptide, nonoligomeric chemical diversity", Proc. Natl. Acad. Sci. USA, Vol. 90, pp. 6909-6913 (August 1993).							
		Koji Suga, et al., "CD98 induces LFA-1-mediated cell adhesion in lymphoid cells via activation of Rap 1", FEBS letters, Vol. 489, pp. 249-253 (2001).							
	Cytokine Ge	Suneet Agarwal and Anjana Rao, et al., "Modulation of Chromatin Structure Regulates Cytokine Gene Expression during T Cell Differentation", Immunity, Vol. 9, pp. 765-775 (December, 1998).							
		Thomas Kamradt, et al., "Tolerance and Autoimmunity", N. Engl. J. Med., Vol. 344, No. 9, pp. 655-664 (March 1, 2001).							
		Wei Li, et al., "Blocked Signal Transduction to the ERK and JNK Protein Kinases in Anergic CD4+ T Cells", Science, Vol. 271, pp. 1272-1276 (March 1, 1996).							
	William L. Pe	William L. Perry, et al., "The itchy locus encodes a novel ubiquitin protein ligase that is disrupted in a 18H mice", Nature Genetics, Vol. 18, pp. 143-146 (February 1998).							
	interleukin 2	Marc K. Jenkins, et al., "Molecular events in the induction of a nonresponsive state in interleukin 2-producing helper T-lymphocyte clones", Proc. Natl. Acad. Sci. USA, Vol. 84, pp. 5409-5413, Immunology (August 1987).							
	Cyrus Choth Immunoglob	Cyrus Chothia, et al., "Canonical Structures for the Hypervariable Regions of Immunoglobulins", J. Mol. Biol., Vol 1996, pp. 901-917 (1987).							
	Ronald H. So The Journal	Ronald H. Schwartz, "Models of T Cell Anergy: Is There A Common Molecular Mechanism", The Journal of Experimental Medicine, Vol. 184, pp. 1-8 (July 1996).							
		Stephen F. Altschul, et al., "Basic Local Alignment Search Tool", J. Mol. Biol., Vol. 215, pp. 403-410 (1990).							
		Steven Xanthoudakis, et al., "An Enhanced Immune Response in Mice Lacking the Transcription Factor NFAT1", Science, Vol. 272, pp. 892-895 (May 10, 1996).							

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<u></u>		OTHER DOCUMEN	T(S) (Including Author, Title, Date,	Pertinent Pages, Etc.)					
	Kenneth M. TCR Thyn	Murphy, et al., nocytes in Vivo	"Induction by Antiger", Science, Vol. 250, p	of Intrathymic pp. 1720-1723 (D	Apoptos ecembe	is of CD4 <sup>.</sup> r 1990).	+CD8+		
	Bart Beverly Internationa	Bart Beverly, et al., "Reversal of <i>in vitro</i> T cell clonal anergy by IL-2 stimulation", International Immunology, Vol. 4, No. 6, pp. 661-671 (March 2, 1992).							
	Vassiiki A. E Transcriptio	Vassiiki A. Boussiotis, et al., "Maintenance of Human T Cell Anergy: Blocking of IL-2 Gene Transcription by Activated Rap1", Science, Vol. 278, pp. 124-128 (October 3, 1997).							
		Ada M. Kruisbeek et al., "Mechanisms underlying T-cell tolerance", Current Opinion in Immunology, Vol. 8, pp. 233-244. (1996).							
	Human Tum	Anne E. Goldfeld, et al., "Identification of a Novel Cyclosporin-sensitive Element in the Human Tumor Necrosis Factor α Gene Promoter", J. Exp. Med., Volume 178, pp. 1365-1379 (October 1993)							
		Patrick E. Fields, et al., "Brocked Ras Activation in Anergic CD4+ T Cells", Science, Vol. 271, pp. 1276-1278 (March 1, 1996).							
	Luika A. Tim	Luika A. Timmerman, et al., "Rapid shuttling of NF-AT in discrimination of Ca <sup>2+</sup> signals and immunosuppression", Nature, Vol. pp. 383, (October 31, 1996).							
		Kurt Bachmaier, et al., "Negative regulation of lymphocyte activation and autoimmunity by the molecular adaptor Cbl-b", Nature, Vol. 403, pp. 211-216 (January 13, 2000).							
	Yungpin J. C	Yungpin J. Chiang, et al., "Cbl-b regulates the CD28 dependence of T-cell activation", Nature, Vol. 403, pp. 216-220 (January 13, 2000).							
	Kevin J. Mal	Kevin J. Maloy, et al., "Regulatorty T cells in the control of immune pathology", Nature							
		Immunology, Vol. 2, No. 9, pp. 816-822 (September 2001).							
	P. Garside, e	et al., "Oral Tol	erance", Seminars in	immunology, Vo	oi. 13, pp	). 1//-185	(2001).		
	Chen Wang, pp. 346-351		s a ubiquitin-depende	nt kinase of MK	K and IK	K", Natur	e, Vol. 412,		
	Orchestration	Ronald N. Germain, et al., "The Dynamics of T Cell Receptor Signaling: Complex Orchestration and the Key Roles of Tempo and Cooperation", Annu. Rev. Immunol., Vol. 17, pp. 467-522 (1999).							

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<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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				<u> </u>				
		OTHER DOCUMENT(S	(Including Author, Title, Date, Pertinent Pages, Etc.)					
	Anjana Rao, et al., "Transcription Factors of the NFAT Family: Regulation and Function", Annu. Rev. Immunol., Vol. 15, pp. 707-747 (1997).							
	Donna M. Berry, et al., "Caspase-dependent cleavage of the hematopoietic specific adaptor protein Gads alters signalling from the T cell receptor", Oncogene Vol. 20, pp. 1203-1211 (2001).							
	proto-oncog	Thomas G. Hofmann, et al., "Caspase-dependent cleavage and inactivation of the Vav1 proto-oncogene product during apoptosis prevents IL-2 transcription", Oncogene Vol. 19, pp. 1153-1163 (2000).						
	Lin Chen, et specifically t	Lin Chen, et al., "Structure of the DNA-binding domains from NFAT, Fos and Jun bound specifically to DNA", Nature, Vol. 392, No. 5, pp. 42-48 (March 5, 1998).						
EXAMINER			DATE CONSIDERED		- <del></del>			

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.